

## Protective effect of *Dalbergia sisso* bark on hepatotoxicity and nephrotoxicity in albino rats

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### ABSTRACT

The aqueous extract of *Dalbergia sisso* bark was screened for its hepatoprotective and nephroprotective activities against paracetamol (300 mg/kg i.p) and CCl<sub>4</sub> (1.0 ml/kg, i.p) induce liver and kidney damage in albino rats. The aqueous extract of *Dalbergia sisso* bark was significantly (\*\*P<0.01) decreased the serum enzyme alanine amino transferase (ALT), asparate amino transferase (AST), alkaline phosphates (ALP), total bilirubin (TB) and significantly increased the total protein (TP) level and significantly increased the levels of SOD, GSH, LPO, CAT. Silymarin (250 mg/kg), a known hepatoprotective and nephroprotective drug used for comparison exhibited significant activity (\*\*P<0.01). The extract did not show any mortality up to a dose of 2000 mg/kg.

**Keywords:** *Dalbergia sisso* Roxb; Carbon tetrachloride, Paracetamol; Hepatoprotective and Nephroprotective activities; Silymarin; Histopathology.

### 1. INTRODUCTION

Inspite of tremendous advances in modern medicine no effective drugs are available, which stimulate liver and kidneys functions and offers protection to the liver and kidneys from the damage or help to regenerate hepatic and nephritic cells (**Chattopadhyay, 2003**). In absence of reliable liver and kidneys - protective drugs in modern medicine, large number of medicinal preparations are recommended for the treatment of liver and kidneys disorders (**Chatterjee, 2000**) and quite often claimed to offer significant relief. Attempts are being made globally to get scientific evidences for these traditionally reported herbal drugs. *Dalbergia sisso* (Roxb) is a climbing creeper and known as *Shisham* in Hindi. The barks are used in jaundice, aphrodisiac, anthelmintic, cure, fever, asthma, high cough, piles, leprosy, inflammation, analgesic, obesity and diabetic (**Kirtikar and Basu, 1999; Fernandopulle and Karunanyake, 1994; Fernandopulle and Ratnasooriya, 1996**).

### 2. Materials and methods

#### 2.1 Plant resources and preparation of crude drug extract

Bark of *Dalbergia sisso* were collected from Salem, Tamilnadu and authenticated by professor, Dr.JAYARAMAN, Ph.D. Director, National institutes of herbal science, Chennai, Tamilnadu. The voucher specimen No ARC/ /2011/1052) was deposited in the herbarium of the National institute of herbal science, Chennai, Tamilnadu. The *Dalbergia sisso* bark was collected and dried for 20 days under shade and cut in small pieces; the small pieces are powdered by using of mechanical grinder. A weighed quantity of powder (500 gm) was passed into sieve number 40 and subjected to aqueous extraction (Maceration) with the distilled water [Distilled water: bark powder] and kept at room temperature for 7 days with occasionally stirring. The extract was filtered. The aqueous extract of *Dalbergia sisso* bark was concentrated in water bath (**Kokane 2001; Sofowora 1993**).

#### 2.2. Phytochemical studies

All the extracts were subjected for phytochemical study (**Khandelwal, 2005**).

#### 2.3. Animals

Male Wistar albino rats of weighing 150-250 grams were selected and procured from Padmavathi college of Pharmacy and Research Institute, Dharmapuri, Tamilnadu. The animals were acclimatized to the standard laboratory conditions in well cross ventilated animal house at temperature  $25 \pm 2^{\circ}\text{C}$  relative humidity 44 –56% and light and dark cycles of 10 and 14 hours respectively for 1 week before and during the experiments. The animals were fed with standard diet and water adlibitum. The experiments were approved by CPCSEA and the institutional animal ethics committee (**Shirwaiker, 1996**).

#### 2.4. Preliminary acute toxicity study

Female rats were divided into 4 groups of six animals each. The control group received saline and the other groups' received 100 to 2000 mg/kg p.o. of test extract respectively. Immediately after dosing, the animals were observed continuously for the first 4 hrs and were observed for 14 days after extract administration to record the mortality.

#### 2.5. Hepatoprotective activity

Hepatic injury was induced in rats by intraperitoneal administration of a single dose of paracetamol (300 mg/kg) and CCl<sub>4</sub> (1.0 ml/kg), olive oil (1.0 ml/kg). Silymarin, a known hepatoprotective agent was used as reference standard. Animals were grouped as follows:

##### 2.5.1. Paracetamol induced hepatotoxicity

**Group I:** Control group, treated with vehicle (2.0 ml, p.o.) daily for 7 days.

**Group II:** Treated with vehicle (2.0 ml, p.o) daily for 7 days followed by paracetamol.

**Group III:** Treated with silymarin (25 mg p.o.) daily for 7 days followed by paracetamol.

**Group IV:** Treated with aqueous extract of *Dalbergia sisso* bark (100 mg/kg p.o.) daily for 7 days followed by paracetamol.

**Group V:** Treated with aqueous extract of *Dalbergia sisso* bark (200 mg/kg p.o.) daily for 7 days followed by paracetamol.

#### **2.5.2. CCL<sub>4</sub> induced hepatotoxicity**

**Group I:** Control group, treated with vehicle (2.0 ml, p.o.) daily for 7 days.

**Group II:** Treated with vehicle (2.0 ml, p.o) daily for 7 days followed by CCL<sub>4</sub>.

**Group III:** Treated with silymarin (25 mg p.o.) daily for 7 days followed by CCl<sub>4</sub> o.

**Group IV:** Treated with aqueous extract of *Dalbergia sisso* bark (100 mg/kg p.o.) daily for 7 days followed by CCl<sub>4</sub>.

**Group V:** Treated with aqueous extract of *Dalbergia sisso* bark (200 mg/kg p.o.) daily for 7 days followed by CCl<sub>4</sub>.

#### **2.6. Nephroprotective activity**

Nephritic injury was induced in rats by intraperitoneal administration of a single dose of paracetamol (300 mg/kg) and CCl<sub>4</sub> (1.0 ml/kg), olive oil (1.0 ml/kg). Silymarin, a known nephroprotective agent was used as reference standard. Animals were grouped as follows:

##### **2.6. 1. Paracetamol induced nephrotoxicity**

**Group I:** Control group, treated with vehicle (2.0 ml, p.o.) daily for 7 days.

**Group II:** Treated with vehicle (2.0 ml, p.o) daily for 7 days followed by paracetamol.

**Group III:** Treated with silymarin (25 mg p.o.) daily for 7 days followed by paracetamol.

**Group IV:** Treated with aqueous extract of *Dalbergia sisso* bark (100 mg/kg p.o.) daily for 7 days followed by paracetamol.

**Group V:** Treated with aqueous extract of *Dalbergia sisso* bark (200 mg/kg p.o.) daily for 7 days followed by paracetamol.

##### **2.6. 2. CCL<sub>4</sub> induced nephrotoxicity**

Group I: Control group, treated with vehicle (2.0 ml, p.o.) daily for 7 days.

Group II: Treated with vehicle (2.0 ml, p.o) daily for 7 days followed by CCL<sub>4</sub>.

Group III: Treated with silymarin (25 mg p.o.) daily for 7 days followed by CCl<sub>4</sub> o.

Group IV: Treated with aqueous extract of *Dalbergia sisso* bark (100 mg/kg p.o.) daily for 7 days followed by CCl<sub>4</sub>.

Group V: Treated with aqueous extract of *Dalbergia sisso* bark (200 mg/kg p.o.) daily for 7 days followed by CCl<sub>4</sub>.

#### **2.7. Statistical analysis**

All the values are expressed as means  $\pm$  S.D. The results were analyzed statistically by Analysis of Variance (ANOVA) followed by Dunnett's comparison test. \*\*P  $\leq$  0.01 were considered significant and \*P  $\leq$  0.01 non-significant.

#### **2.7. Biochemical Studies**

At the end of the treatment, blood samples of each animal were collected in epindroff tubes allowed to clot. Serum was separated and used for the assay of marker enzymes viz., alanine amino transferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and total bilirubin (TB) and total protein (TP). Estimation of antioxidant enzymes (CAT, SOD, LPO, GSH)

#### **2.8. Histopathology studies:**

Liver and kidney were excised from the experimental animals of each group and washed with normal saline solution. Initially the materials were fixed in 10% buffered neutral formalin for 48 hrs and then with bovine solution for 6 hrs. They were then processed for paraffin embedding. The sections were taken at 5  $\mu$ m thickness using microtome, processed in alcohol-xylene series and stained with haematoxylin and eosin. These sections were examined microscopically for the evaluation of histopathological changes.

### **3. Results and discussion**

#### **3.1. Preliminary Phytochemical Analysis**

The percentage yield of aqueous extract of *Dalbergia sisso* bark was found to be 6.0 % w/w. The qualitative phytochemical analysis of the aqueous extract showed the presence of carbohydrates, proteins, amino acids, flavanoids, glycosides, tannins, saponins and phenolic compounds.

#### **3.2. Pharmacology evaluation**

##### **3.2.1. Effect of aqueous extract of DSB on Acute Toxicity Study**

None of the 5 rats died or showed any sign of toxicity at the limit dose of 2000 mg/kg oral in the first 48 hours and no evidence of toxicity was noted during the period of 14 days observation. It was observed that the test extract was not mortal even at 2000 mg/kg dose. Hence, 100 mg/kg and 200 mg/kg of this dose were selected for further study.

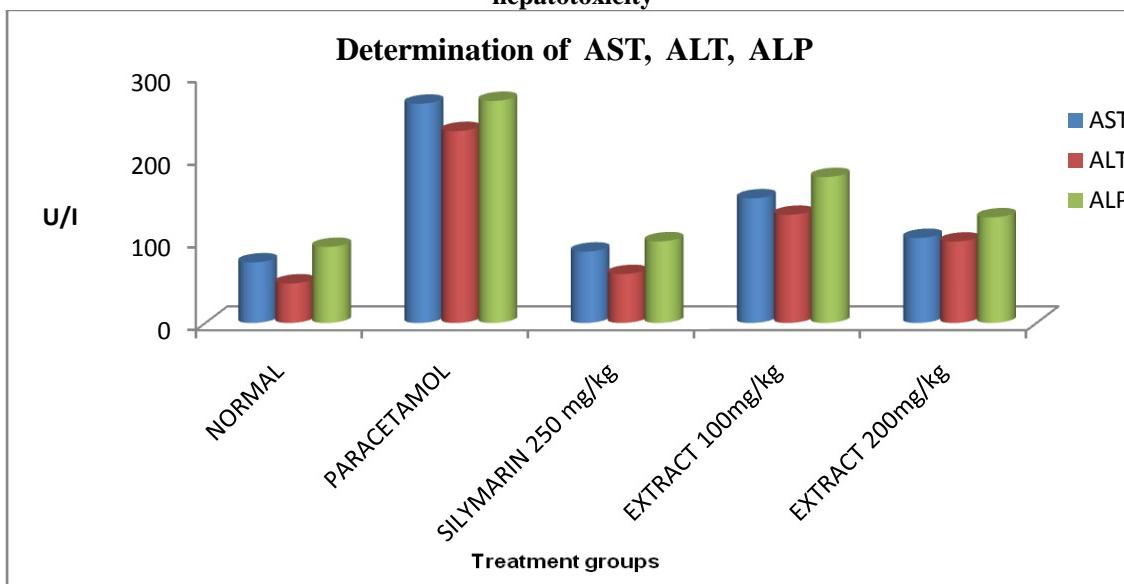
**Table 1.**Effect of aqueous extract of *Dalbergia sisso* bark on AST, ALT, ALP, TB and TP against paracetamol induced hepatotoxicity

| Treatment  | AST<br>(U/I)        | ALT<br>(U/I)       | ALP<br>(U/L)         | Total<br>bilirubin<br>(mg/ml ) | Total protein<br>(gm/dl) |
|--|---------------------|--------------------|----------------------|--------------------------------|--------------------------|
| Group-I<br>(Normal control)                          | 73.32 ±<br>2. 60    | 47.81 ±<br>2. 23   | 92.05 ±<br>3. 89     | 1.36 ±<br>0. 08                | 7.98 ±<br>0. 09          |
| Group-II<br>(Paracetamol 300 mg/kg i.p)              | 265.38 ±<br>3.98*   | 232.36 ±<br>4.12*  | 268.82 ±<br>4. 98*   | 4.82 ±<br>0.05*                | 3.02 ±<br>6. 82*         |
| Group-III<br>(Silymarin 250 mg/kg+ paracetamol)      | 86.37 ±<br>2. 20**  | 59.18 ±<br>3.6**   | 98.81 ±<br>3.73**    | 1.62 ±<br>0.04**               | 7.03 ±<br>0.03**         |
| Group-IV<br>(Aqueous extract 100 mg/kg+ Paracetamol) | 150.81 ±<br>3. 87** | 130.92 ±<br>4.21** | 176.65 ±<br>11.42 ** | 2.56 ±<br>0.06**               | 5.82 ±<br>0. 06**        |
| Group-V<br>Aqueous extract 100 mg/ kg+ Paracetamol)  | 102.91 ±<br>4. 62** | 98.46 ±<br>2. 52** | 127.86 ±<br>8.10**   | 2.77 ±<br>0.05**               | 6.02 ±<br>0. 06**        |

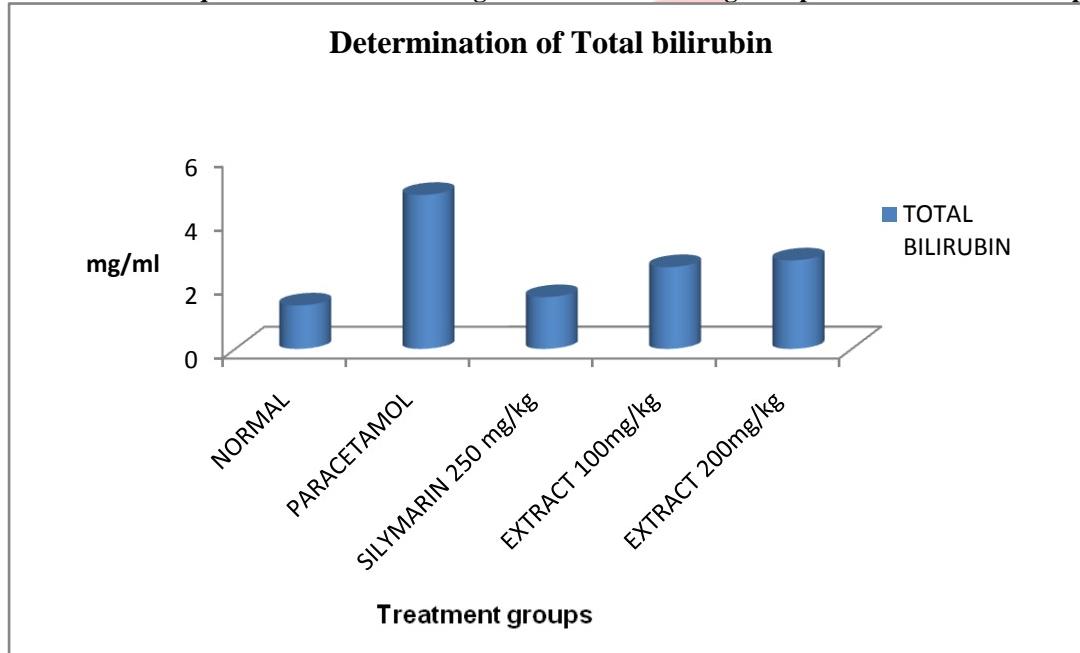
The results are expressed as mean ± S.E.M. (n=6) \*P < 0.01 Group II compared with Group I and \*\*P < 0.01 Group III, Group IV, Group V compared with Group II. Where the significance was performed by One way ANOVA followed by Dunnett's comparison test.



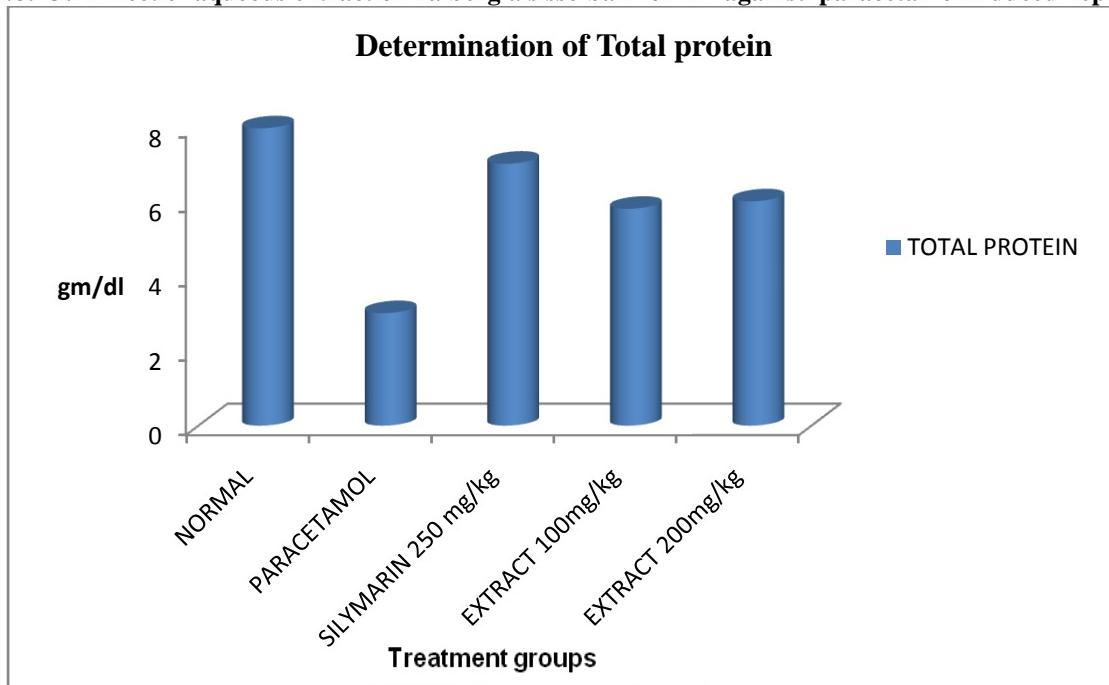
**Graph No.1:- Effect of aqueous extract of Dalbergia sisso bark on AST, ALT and ALP against paracetamol induced hepatotoxicity**



**Graph No. 2:- Effect of aqueous extract of Dalbergia sisso bark on TB against paracetamol induced hepatotoxicity**



**Graph No. 3:- Effect of aqueous extract of Dalbergia sisso bark on TP against paracetamol induced hepatotoxicity**

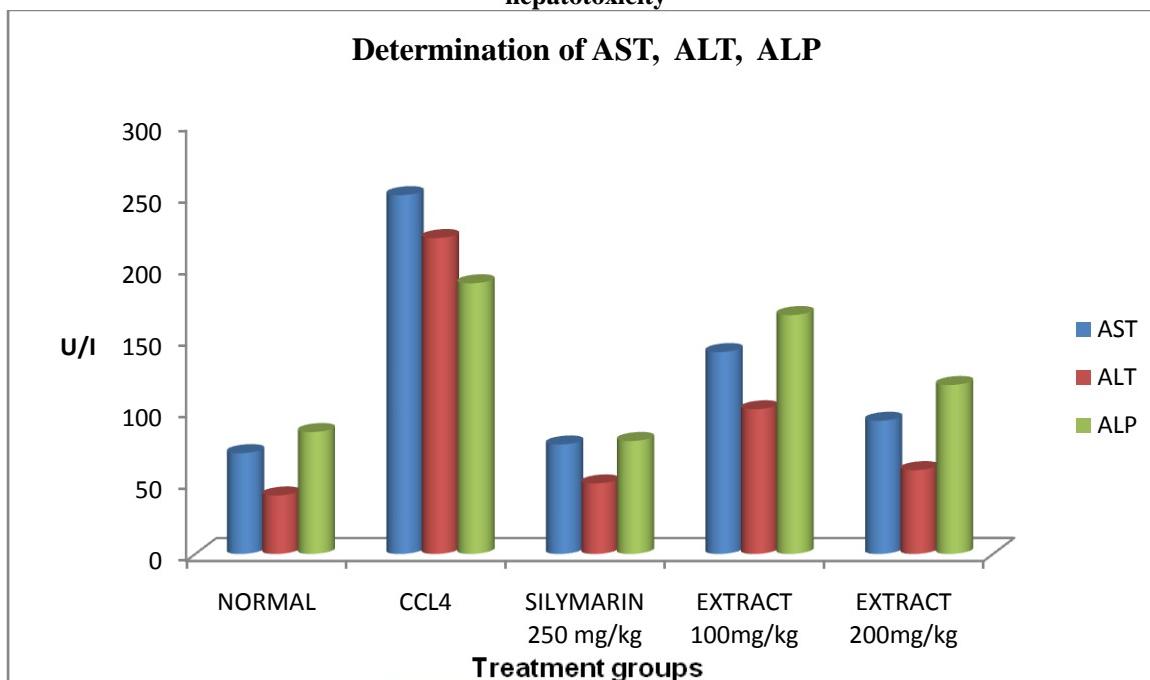


**Table No. 4:- Effect of aqueous extract of *Dalbergia sisso* bark on AST, ALT, ALP, TB and TP against CCL<sub>4</sub> induced hepatotoxicity**

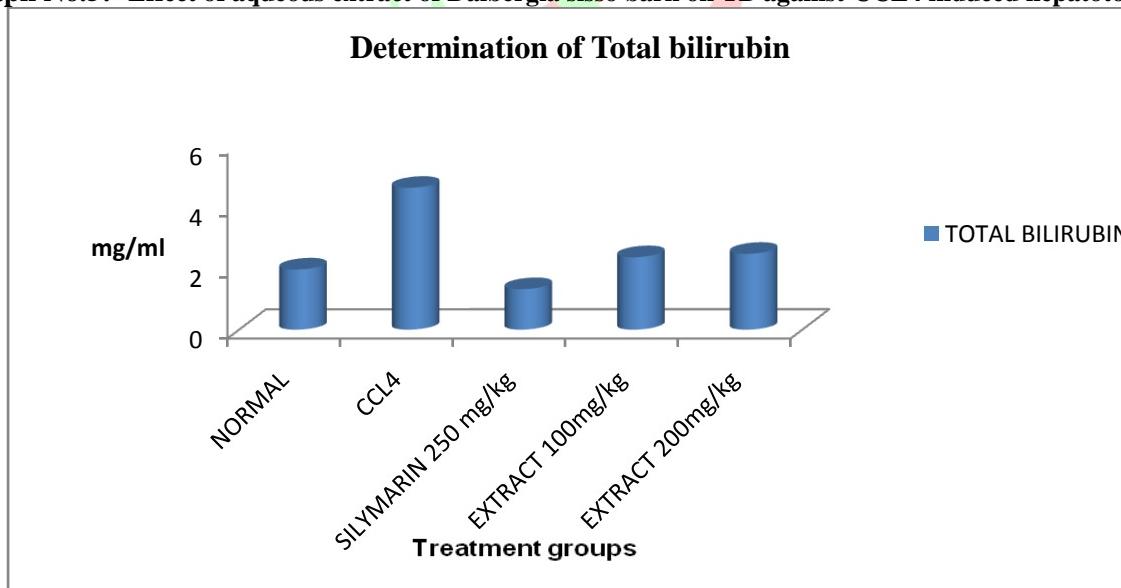
| Treatment  | AST<br>(U/I)       | ALT<br>(U/I)       | ALP<br>(U/L)         | Total<br>bilirubin<br>(mg/ml ) | Total protein<br>(gm/dl) |
|--|--------------------|--------------------|----------------------|--------------------------------|--------------------------|
| Group-I<br>(Normal control )                                     | 70.32 ±<br>2.50    | 40.81 ±<br>2.13    | 85.05 ±<br>2.89      | 1.96 ±<br>0.08                 | 6.78 ±<br>0.08           |
| Group-II<br>(CCL <sub>4</sub><br>300 mg/ kg i.p)                 | 250.28 ±<br>3.88 * | 220.36 ±<br>4.12 * | 188.81 ±<br>4.78 *   | 4.62 ±<br>0.05 *               | 4.03 ± 5.82*             |
| Group-III (Silymarin<br>250 mg/ kg+ CCL <sub>4</sub> )           | 76.37 ±<br>2.20**  | 40.18 ±<br>3.6**   | 78.81 ± 3.73**       | 1.32 ± 0.04**                  | 6.03 ± 0.03**            |
| Group-IV<br>(Aqueous<br>extract 100 mg/kg+<br>CCL <sub>4</sub> ) | 140.81 ±<br>3.87** | 100.92 ± 4.31**    | 166.65 ± 11.32<br>** | 2.36 ±<br>0.06**               | 2.62 ± 0.05**            |
| Group-V<br>(Aqueous extract 200 mg/kg+ CCL <sub>4</sub> )        | 92.91 ±<br>4.62**  | 58.46±<br>2.52**   | 117.86 ±<br>7.10**   | 2.47 ± 0.05**                  | 4.02 ± 0.06**            |

The results are expressed as mean ± S.E.M. (n=6) \*P < 0.01, Group II compared with Group I and \*\*P < 0.01 Group III, Group IV, Group V compared with Group II Where the significance was performed by One way ANOVA followed by Dunnett's comparison test.

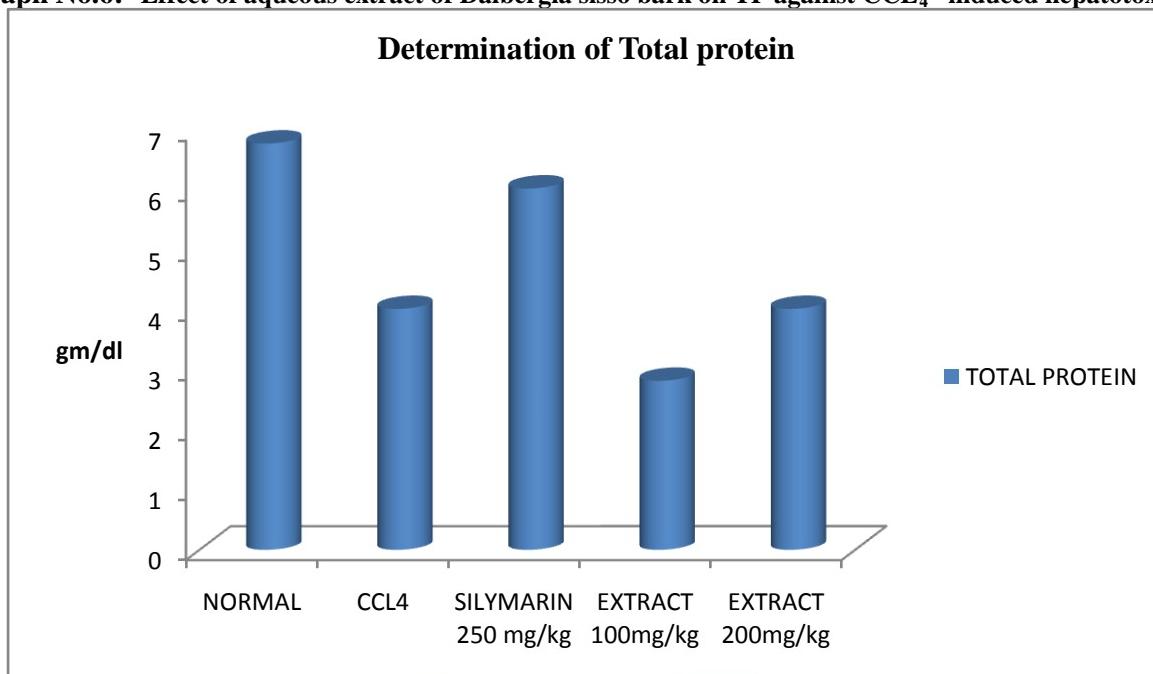
**Graph No.4:- Effect of aqueous extract of Dalbergia sisso bark on AST, ALT and ALP against CCL<sub>4</sub> induced hepatotoxicity**



**Graph No.5:- Effect of aqueous extract of Dalbergia sisso bark on TB against CCL4 induced hepatotoxicity**



**Graph No.6:- Effect of aqueous extract of *Dalbergia sisso* bark on TP against CCL<sub>4</sub> induced hepatotoxicity**

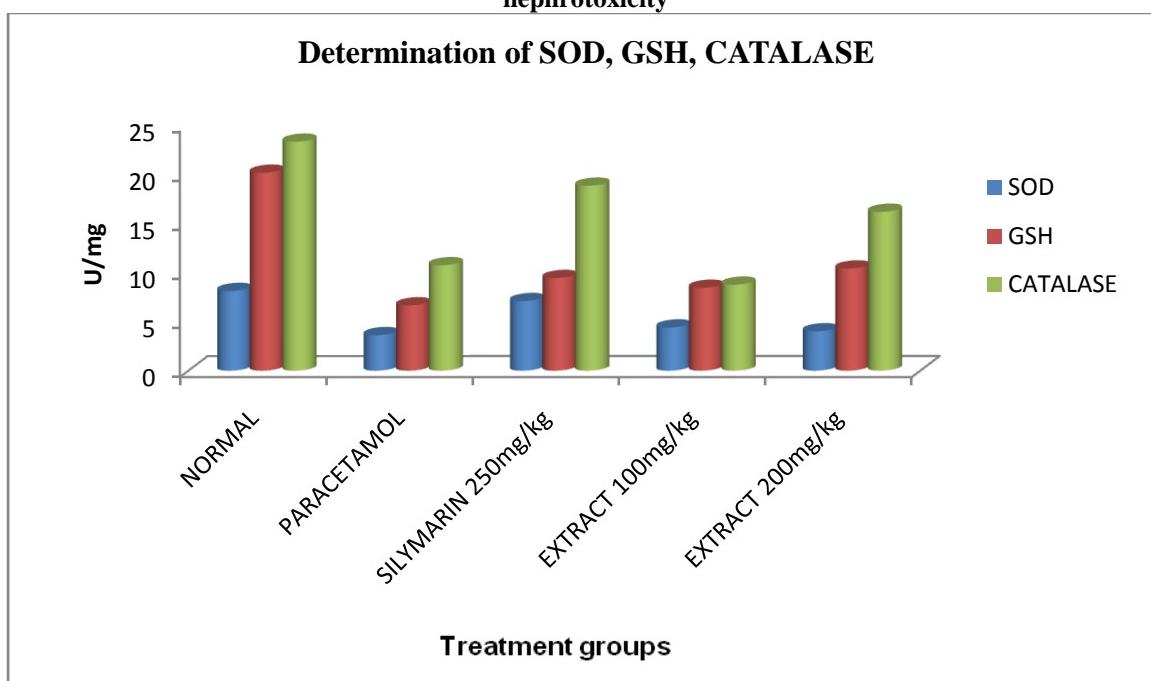


**Table No.5:- Effect of aqueous extract of *Dalbergia sisso* bark on SOD, GSH, CAT and LPO against paracetamol induced nephrotoxicity**

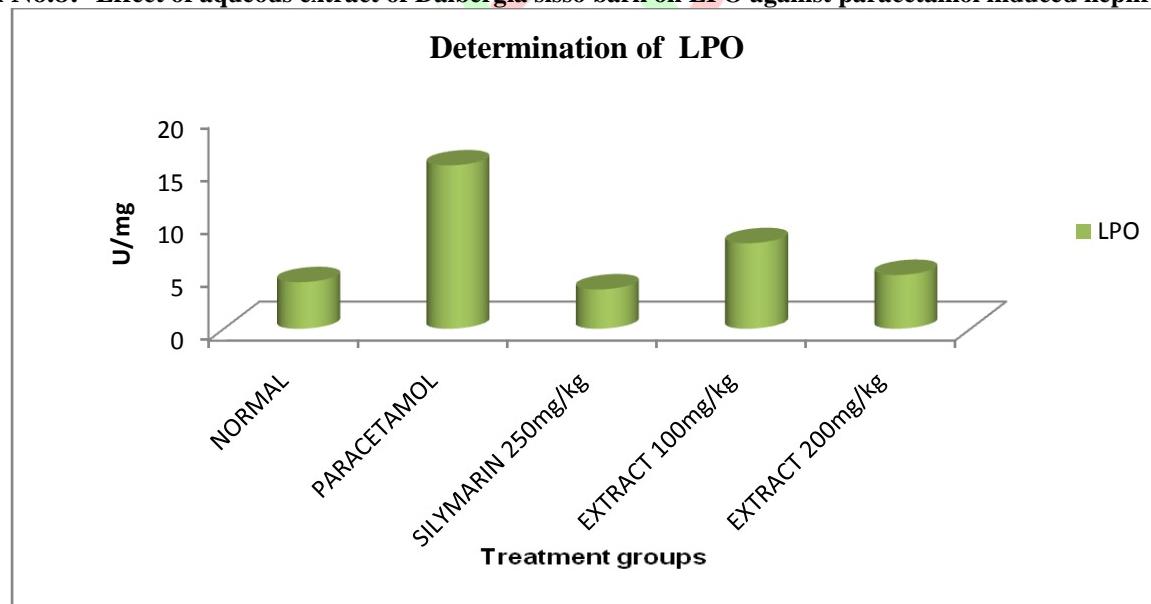
| Treatment   | LPO<br>(units/mg<br>protein) | SOD (units/mg<br>protein) | GSH<br>(units/mg<br>protein) | CATALASE<br>(units/mg<br>protein) |
|---|------------------------------|---------------------------|------------------------------|-----------------------------------|
| Group-I<br>(Normal control)                               | 4.38 ± 0. 46                 | 8.12 ± 0. 29              | 20.16 ± 0. 98                | 23.32 ± 1. 80                     |
| Group-II<br>(paracetamol<br>300 mg/kg i.p)                | 15.37 ± 0. 98*               | 3.62 ± 0.15*              | 6.65 ± 0. 57*                | 10.74 ± 0. 66*                    |
| Group-III<br>Silymarin 250 mg/kg +<br>paracetamol         | 3.70 ± 3. 22 **              | 7.09 ± 0.40**             | 9.44 ± 0. 66**               | 18.84 ± 0. 61*                    |
| Group-IV<br>(Aqueous extract 100 mg/ kg<br>+ paracetamol) | 8.05 ± 0. 57**               | 4.40 ± 0. 39**            | 8.44 ± 0. 55**               | 8.76 ± 0. 51**                    |
| Group-V<br>(Aqueous extract 200 mg/ kg<br>+ paracetamol)  | 5.06 ± 0. 40**               | 4.01 ± 0. 22**            | 10.41 ± 0. 60**              | 16.18 ± 0. 37 *                   |

The results are expressed as mean ± S.E.M. (n=6) \*P < 0.01, Group II compared with Group I and \*\*P < 0.01 Group III, Group IV, Group V compared with Group II. Where the significance was performed by One way ANOVA followed by Dunnett's comparison test.

**Graph No.7:- Effect of aqueous extract of *Dalbergia sisso* bark on SOD, GSH and CAT against paracetamol induced nephrotoxicity**



**Graph No.8:- Effect of aqueous extract of *Dalbergia sisso* bark on LPO against paracetamol induced nephrotoxicity**

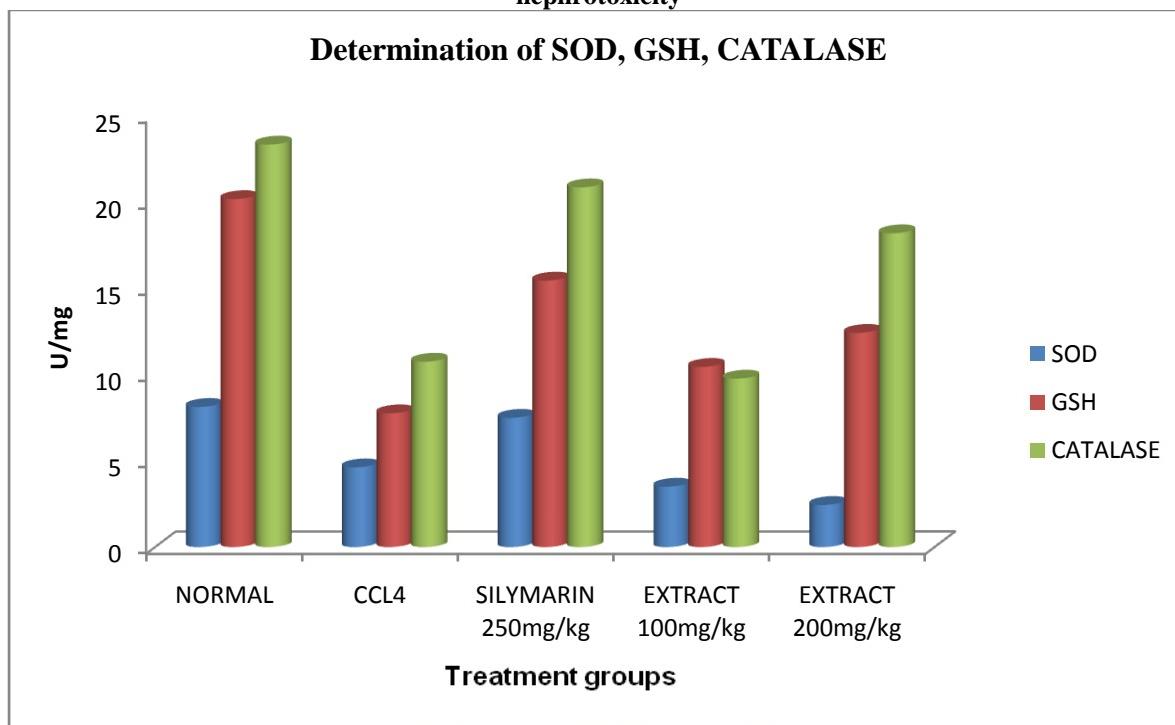


**Table No.6:- Effect of aqueous extract of *Dalbergia sisso* bark on SOD, GSH, CAT, and LPO against CCL<sub>4</sub> induced nephrotoxicity**

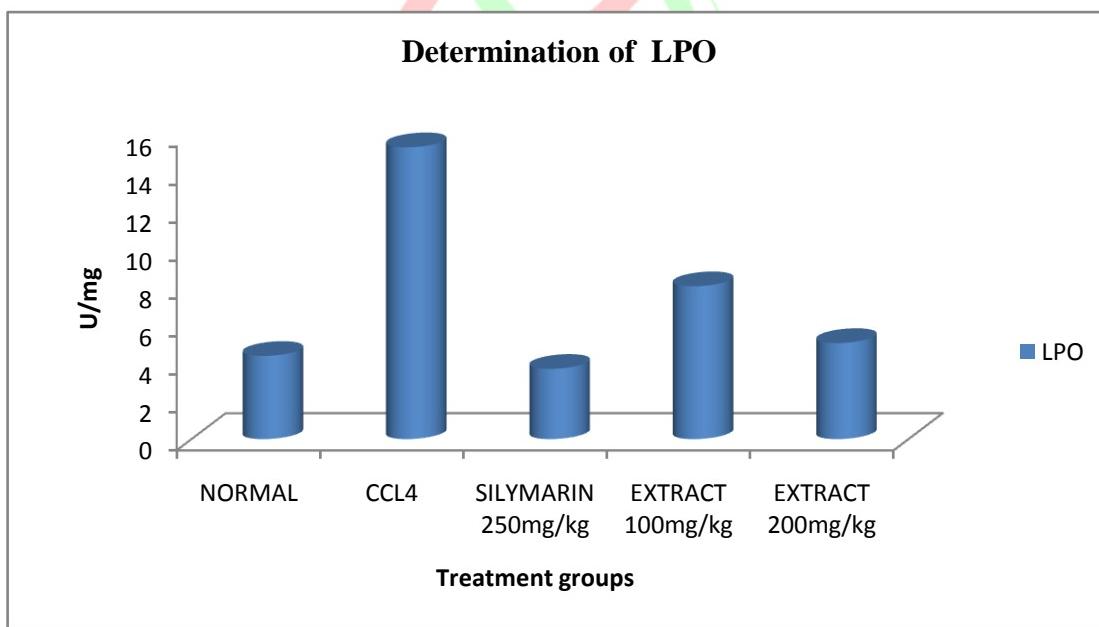
| Treatment  | LPO<br>(units/mg<br>protein) | SOD<br>(units/mg<br>protein) | GSH<br>(units/mg<br>protein) | CATALASE<br>(units/mg<br>protein) |
|--|------------------------------|------------------------------|------------------------------|-----------------------------------|
| Group-I<br>(Normal control)                                  | 6.48 ± 0. 56                 | 10.12 ± 0.39                 | 24.26 ± 0. 88                | 26.42 ± 2. 80                     |
| Group-II<br>(CCL <sub>4</sub> 1 ml/ kg i.p)                  | 25.47 ± 0. 98*               | 5.62 ± 0. 15*                | 6.65 ± 0. 57*                | 10.74 ± 0. 66*                    |
| Group-III<br>(Silymarin 250 mg/kg + CCL <sub>4</sub> )       | 5.80 ± 4. 22 **              | 9.09 ± 0. 40**               | 9.44 ± 0. 66**               | 18.84 ± 0. 61**                   |
| Group-IV<br>(Aqueous extract 100 mg / kg+ CCL <sub>4</sub> ) | 10.08 ± 0. 67**              | 7.40 ± 0. 39**               | 8.44 ± 0. 55**               | 8.76 ± 0. 51**                    |
| Group-IV<br>(Aqueous extract 200 mg/kg+ CCL <sub>4</sub> )   | 8.07 ± 0. 50**               | 8.44 ± 0. 22**               | 10.41 ± 0. 60**              | 16.18 ± 0. 37**                   |

The results are expressed as mean ± S.E.M. (n=6) \*P < 0.01, Group II compared with Group I and \*\*P < 0.01 Group III, Group IV, Group V compared with Group II. Where the significance was performed by One way ANOVA followed by Dunnett's comparison test.

**Graph No.9:- Effect of aqueous extract of Dalbergia sisso bark on SOD, GSH and CAT against CCL<sub>4</sub> induced nephrotoxicity**



**Graph No.10:- Effect of aqueous extract of Dalbergia sisso bark on LPO against CCL<sub>4</sub> induced nephrotoxicity**



### 3.3. Histopathology changes of liver

#### 3.3.2. Effect of Dalbergia sisso bark on liver of rats against paracetamol induced hepatotoxicity

##### Fig. No. A Normal control

Showed Liver with normal hepatocytes (40X)

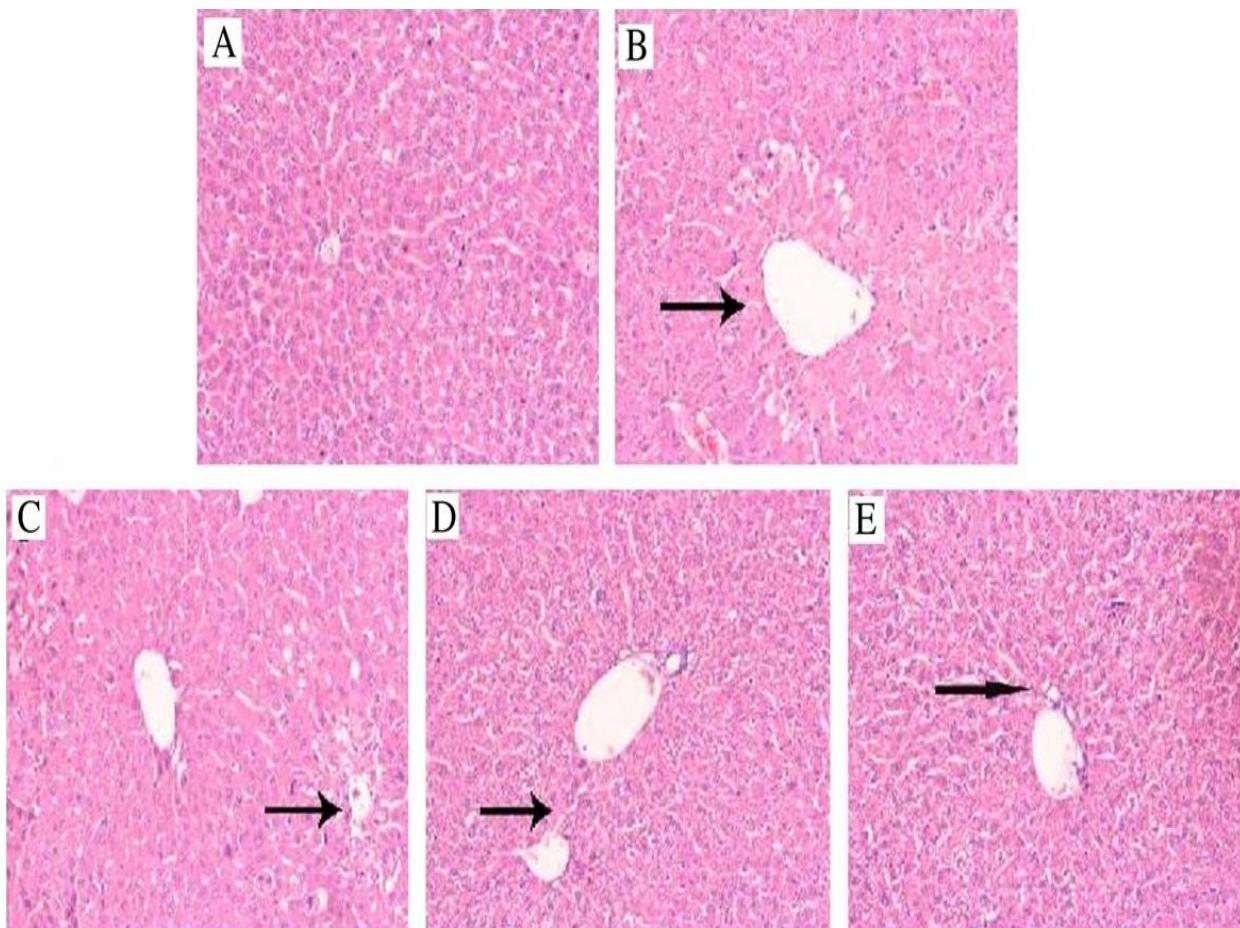
##### Fig. No. B. Paracetamol (300 mg /kg)

Showed lymphatic infiltration around the bile duct. Also note the degeneration of hepatocytes and mild cirrhosis in the portal area. (40X)

**Fig. No. C. Silymarin (250 mg / kg) + paracetamol (300 mg / kg)**  
Showed the degenerative change and occasional lymphocytes.

**Fig. No. D. ADSB (100 mg / kg) + paracetamol (300 mg / kg)**  
Showed the total normal appearance of hepatic parenchyma (40X)

**Fig. No E. ADSB (200 mg / kg) + paracetamol (300 mg / kg)**  
Showed normal hepatocytes and congenital sinusoids (40X)



#### . Effect of ADSB on histopathological change against paracetamol induced hepatotoxicity

Histopathological profile of liver sections of normal group showed normal cellular architecture with distinct hepatic cells, sinusoidal spaces and central vein (**Figure No. A**). The normal architecture of liver was completely lost in rats treated with paracetamol (**Figure No. B**) with the appearance of vacuolated hepatocytes and degenerated nuclei.

Vacuolization, fatty changes and necrosis of hepatocytes were severe in the centrilobular region. Paracetamol toxicity led to excessive formation of deposition of connective tissue. Whereas treatment with ADSB (100 and 200 mg/kg) and silymarin (250 mg/kg) showed regeneration of hepatic cells (**Figure No. C, D, E**).

#### 3.3.3. Effect of *Dalbergia sisso* bark on liver of rats against CCl<sub>4</sub> induced hepatotoxicity

##### **Fig. No. A Normal**

Normal hepatocytes (40X)

##### **Fig. No.B CCL4 (1.0 ml / kg)**

Showed lymphatic infiltration around the bile duct. Also note the degeneration of hepatocytes and mild cirrhosis in the portal area. (40X)

##### **Fig. No. C Silymarin (250 mg / kg) + CCL4 (1.0 ml / kg)**

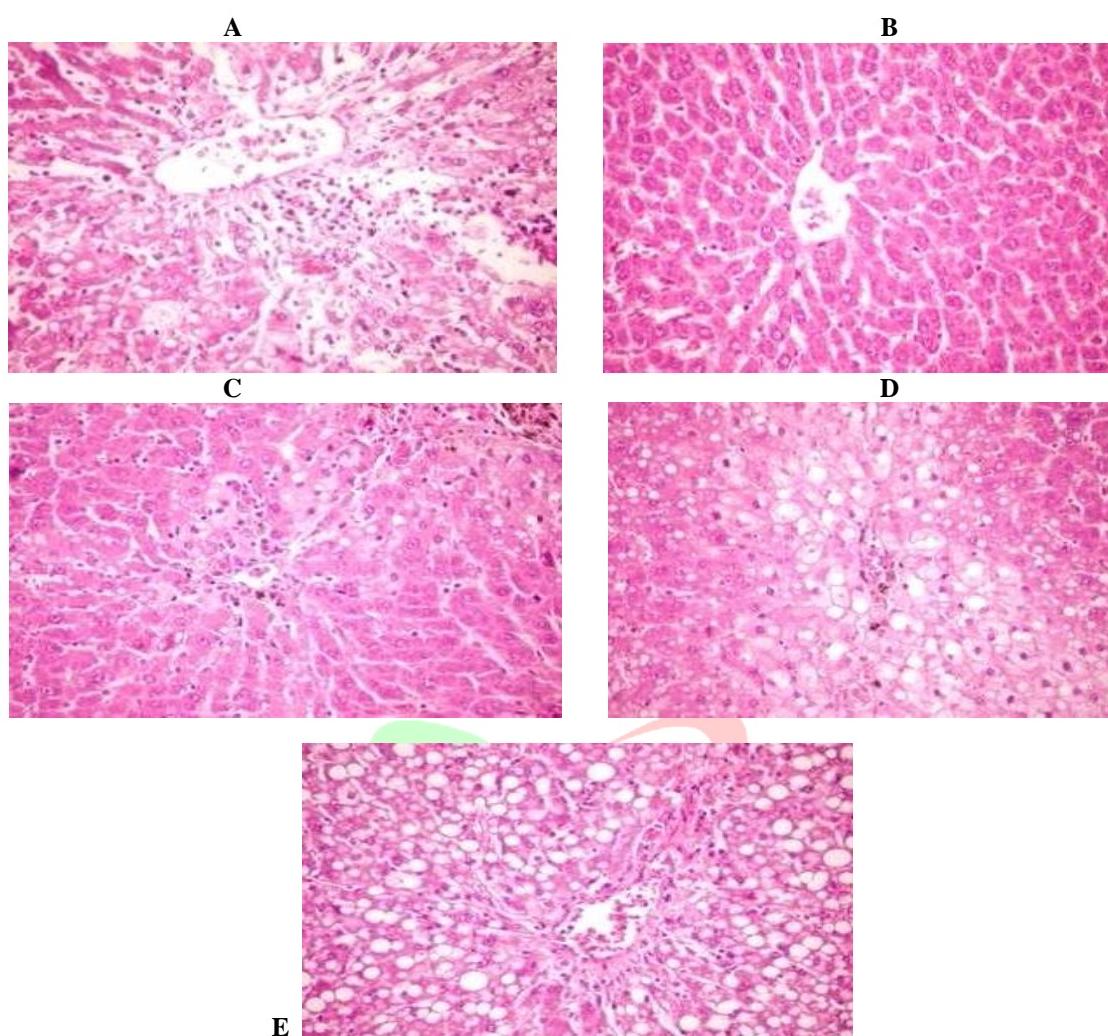
Showed the degenerative change and occasional lymphocytes.

##### **Fig. No. 13 ADSB (100 mg / kg) + CCL4 (1.0 ml / kg)**

Showed the total normal appearance of hepatic parenchyma (40X)

##### **Fig. No. 14 ADSB (200 mg / kg) + CCL4 (1.0 ml / kg)**

Showed normal hepatocytes and congenital sinusoids (40X)



#### **Effect of ADSB on histopathological change against $\text{CCl}_4$ induced hepatotoxicity**

Histopathological profile of liver sections of normal group showed normal cellular architecture with distinct hepatic cells, sinusoidal spaces and central vein (**Figure No. A**). The normal architecture of liver was completely lost in rats treated with  $\text{CCl}_4$  (**Figure No. B**) with the appearance of vacuolated hepatocytes and degenerated nuclei.

Vacuolization, fatty changes and necrosis of hepatocytes were severe in the centrilobular region. Paracetamol toxicity led to excessive formation of deposition of connective tissue. Whereas treatment with ADSB (100 and 200 mg/kg) showed significant hepatoprotective activity (**Figure No. C, D**) and silymarin (250 mg/kg) also showed significant protection (**Figure No. E**) (Janbazand Gilani, 2000).

#### **3.3.4. Effect of *Dalbergia sisso* bark on kidney of rats against paracetamol induced nephrotoxicity**

##### **Fig. No. 15 Normal**

The normal histopathological structure of renal parenchyma (40X)

##### **Fig. No.16 Paracetamol (300 mg / kg)**

Showed vacuolations of endothelial lining and Glomerular tufts as well as epithelial lining renal tubules (40X)

##### **Fig. No. 17 Silymarin (250 mg /kg) + Paracetamol (300 mg / kg)**

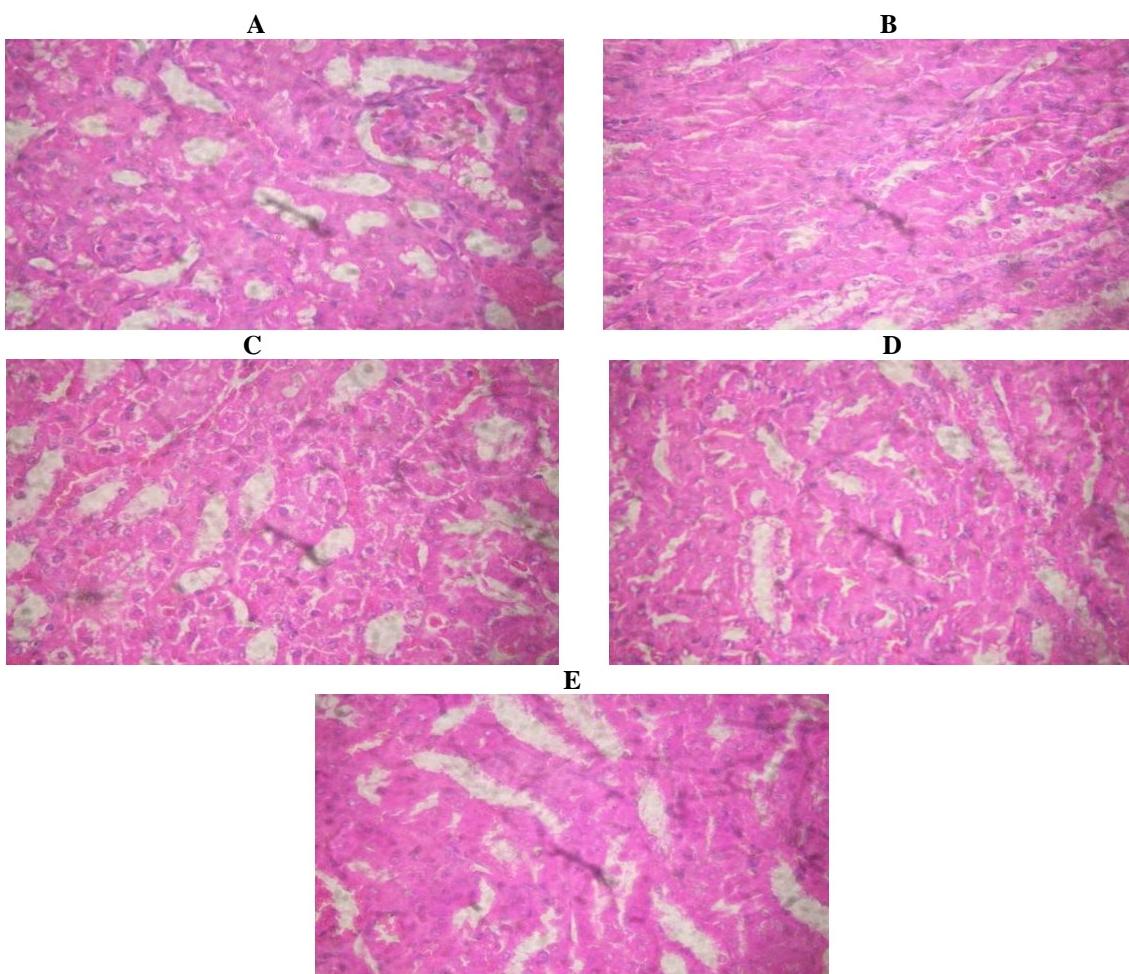
The normal histopathological structure of renal parenchyma (40X)

##### **Fig. No.18 ADSB (100 mg / kg) + Paracetamol (300 mg /kg)**

Showed normal structure of renal parenchyma and epithelial lining (40 X)

##### **Fig. No. 19 ADSB (200 mg /kg) + Paracetamol (300 mg / kg)**

Showed normal renal tubules (40X)



#### **Effect of ADSB on histopathological change against paracetamol induced nephrotoxicity**

Haematoxylin and eosin stained sections of the cortex of the kidney in normal group showed presence of the glomeruli which consists of a tuft of blood capillaries surrounded by capsular space and Bowman's capsule (**Fig. No. A**). The cortex of the kidney in paracetamol treated rats showed the histopathological changes were mainly in the cortico medullary region.

All types of cortical renal tubules were affected with different degree of damage. The most severely affected were the proximal convoluted tubules and distal convoluted tubules. The animals showed degenerative changes in the form of vacuolated cytoplasm (**Fig. No. B**).

Whereas treatment with ADSB (100 and 200 mg/kg) and silymarin (250 mg/kg) the cortex of the kidney showed normal structure similar to that of normal group. When compared to paracetamol -treated group, there were statistical significant decreases regarding degenerative and necrotic changes in proximal convoluted tubules and distal convoluted tubules (**Fig. No. C, D, E**).

#### **3.3.5. Effect of Dalbergia sisso bark on kidney of rats against CCl<sub>4</sub> induced nephrotoxicity**

##### **Fig. No. 21 Normal**

Showed normal of epithelial lining and some renal tubules (40 X)

##### **Fig. No. 22 CCl<sub>4</sub> (1.0 ml / kg)**

Showed the vacuolization of epithelial (40 X)

##### **Fig. No.23 Silymarin (250 mg / kg) + CCl<sub>4</sub> (1.0 ml / kg)**

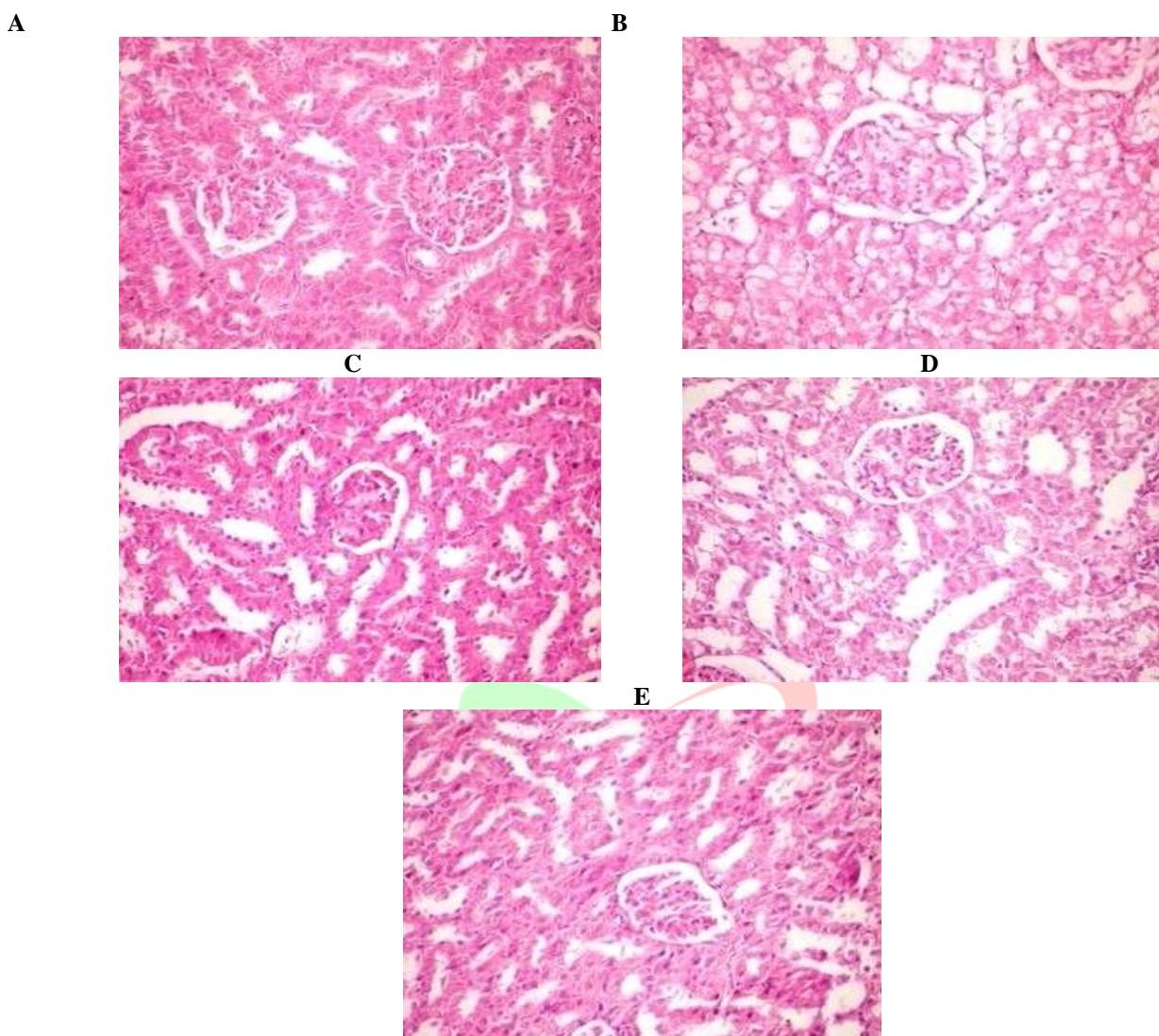
Normal of epithelial lining and some renal tubules (40 X)

##### **Fig. No. 24 ADSB (100 mg / kg) + CCl<sub>4</sub> (1.0 ml / kg)**

Vacuolization of epithelial showed normal (40 X)

##### **Fig. No. 25 ADSB (200 mg / kg) + CCl<sub>4</sub> (1.0 ml / kg)**

Showed the no vacuolization of epithelial (40 X)



#### 4.DISCUSSION

In the present study, we have evaluated the hepatoprotective and nephroprotective effect of bark of *Dalbergia sisso* against paracetamol and  $\text{CCl}_4$  induced acute hepatotoxicity and nephrotoxicity in rats. i. p. injection of  $\text{CCL}_4$  and  $\text{CCl}_4$  induced liver and kidney damage that was revealed by significant increase in serum levels and induced toxicity by bio activation, primarily through the activity of CYP2E1 and by the generation of free radicals. (**Drotman and Lawhorn, 1978**).

The phytochemical studies revealed the presence of phenols, tannins, flavanoids, steroids & terpenoids. These components may be responsible for hepatoprotective and nephroprotective activities (**Janbazand Gilani, 2000**).

These free radicals initiate lipid peroxidation by abstracting a hydrogen atom from the polyunsaturated fatty acid of a phospholipids' (**Recknagel et al., 1989; Weber et al., 2003**).

Paracetamol and Carbon tetrachloride-induced lipid peroxidation increases the permeability of the plasma membrane to  $\text{Ca}^{2+}$ , leading to severe disturbances of calcium homeostasis and necrotic cell death (**Weber et al., 2003**). This was further substantiated liver and kidney cell necrosis and plays a significant role in accumulation, depletion of serum marker enzymes(ALT,AST,ALP,TP and TB) and antioxidant enzymes (GSH,SOD,CAT and LPO) (**Ploa and Hewitt, 1989**). Depression of protein synthesis and loss of enzymes activity (**Recknagel et al., 1989**).

Administration of Paracetamol (300mg/kg) and  $\text{CCL}_4$  (1.0ml/kg) are in high dose to rats produced hepatotoxicity and nephrotoxicity showed by significant increased (\*  $P < 0.01$ ) in the serum levels of ALT, AST and ALP, TB and significant (\*  $P < 0.01$ ) reduction in total protein content (**James and Pickering, 1976**).And significant (\* $p < 0.01$ ) decrease SOD and CAT and GSH levels in rats. LPO significantly increased (\* $p < 0.01$ ) in  $\text{CCL}_4$  and  $\text{CCL}_4$  treated rats when compared to normal rats (**Recknagel et al., 1989**).

#### 5. CONCLUSION

On the basis of results obtained, it can be concluded that the aqueous extract of *Dalbergia sisso* bark seems to possess hepatoprotective and nephroprotective activities in rats. No toxic symptom or mortality was observed in 14 days of study in rats. Histopathological examination of the liver and kidney section of the rats treated with toxicant showed intense

centrilobular necrosis and vacuolization. The rats treated with aqueous extract of *Dalbergia sisso bark* (100 mg/kg and 200 mg/kg) along with toxicant showed sign of protection against these toxicants to considerable extent as evident from absence of necrosis and vacuoles.

Further studies are required to illustrate the mechanism of action and isolation of active principle of aqueous extract of *Dalbergia sisso bark* for hepatoprotective and nephroprotective activities.

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